TPQ Consultancy

The Role of the Qualified Person for Clinical Trials in the European Union

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Before we begin…

… The Requirements for any Clinical Trial

The safeguarding of the clinical trial subject has to be ensured by guaranteeing the quality and safety of the products and substances used in the trial.

- Helsinki Declaration

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So…why do you need a QP?

Because you want (need) to get your Clinical Trial going in Europe – and keep it going

So what can you do to facilitate this process?

Provide what the QP needs

But what does the QP need?

Understand the role and responsibilities of the QP

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But, first....What is a QP?

- ‘A QP has to use their technical knowledge of all aspects of manufacture and control, needs to have skills in working with others and make judgments based on the information available'.

- 'The role of the QP is like that of a conductor of an orchestra. The QP needs to manage, coordinate and understand what's happening and then cajole/encourage where required to get the best possible results!’

- ‘A QP is like a 'rhinoceros' - thick skinned, broad shouldered and always with a definite point‘!

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Seriously…What is a QP?

- **Qualified Person (QP)**
  - Technical term used in European Union (EU) pharmaceutical regulation
  - First established in 1975
  - Unique regulatory requirement applicable within the EU and Member States of the European Economic Area (EEA).
  - The requirement for QP covers both Human (Clinical and Commercial) and Veterinary Medicinal Products including those intended for export.

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A QP is…

- A QP's main responsibility in pharmaceuticals production is to ensure that each batch of a medicinal product has been produced and tested in accordance with the EU Directives, Good Manufacturing Practices (GMP) and the provision of the approved IMPD and CTA for Clinical medicinal products.
- The significance of the QP's position in Europe is clearly demonstrated by the extensive legal basis this position.

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A QP is… finally!

Under the permanent provisions of the EU legislation (2001/83/EC) a QP is:

- Typically, a licensed pharmacist, biologist or chemist (other academic qualifications are permitted);
- Typically has several years experience working in pharmaceutical manufacturing operations;
- Passed examinations confirming his or her knowledge and ability.
- A resident of the EU

- **Each Qualified Person has a personal and professional responsibility for being certain that the all checks and tests on the medicinal product under review have been carried out.**

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So…how is this done?

A Qualified Person certifying a batch for release always has to ensure that , amongst others, the following requirements have been met:

1. The Marketing Authorisation and Manufacturing Authorisation or Investigational Medicinal Products Authorisation requirements for the Medicinal Products have been met for the batch concerned.

2. The principles and guidelines of GMP as stated in Directive 2003/94/EC (Human) or Directive 91/412/EEC (Veterinary) and as interpreted in the EU Guide to GMP have been followed or that the medicinal products have been manufactured in accordance with GMP standards which are at least equivalent to those of the EU or EEA

3. The principal manufacturing and testing processes have been validated – depending on the type of IMP.

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Clinical Trial in the EU

Fundamentals

- Why do your Clinical Trial in the EU?
- What is different about a Clinical Trial in the EU?
- How do you run a Clinical Trial and provide IMP for a Clinical Trial in the EU?
- What can you do to facilitate the process?

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Why the EU?

Due to narrowed therapeutic application / specific indications, there has been an increase in global/trans-Atlantic clinical trials to increase statistical data to support new/improved therapy.

Population hetrogenicity of the EU is similar to the United States

The UK provides a ‘common’ language environment to facilitate entry for US based clients

BUT … What will Brexit mean to my Clinical Trial?

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What is different in the EU?

Implementation of EU Regulation No 536/2014

Regulatory & Ethics Approvals

- Clinical Trials Application
- Investigational Medicinal Product Dossier (IMPD)
    - Must include QP Declaration
- Investigator/Study Protocol

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How do you run a Clinical Trial in the EU?

Supply of IMP

- Manufacture – GMP and IMPD
- Testing - GMP and IMPD
    - Release testing (EU Import)
    - Post-pack Identity testing
- Packing – GMP and IMPD
    - Packaging materials
        - Primary Contact
        - Labeling

Special Precautions – GMP meets R&D

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How do you run a Clinical Trial in the EU?

Active Pharmaceutical Ingredient (API)

- Must be manufactured in compliance with Part II of the EU GMP Guidelines
  - Chemical – Validation of process completed prior to Phase III
  - Biological – Process must be fully validated

Drug Product

- Must be manufactured in compliance with Part I of the EU GMP Guidelines
  - Chemical – Validation of process completed prior to Phase III
  - Biological – Process must be fully validated

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Facilitating the Process

Requirement for a QP occurs at two distinct points in the documentation process

- Application process
- Drug Product release and certification

Regulatory & Ethics

- Clinical Trials Application
- Investigator/Study Protocol
- Investigational Medicinal Product Dossier (IMPD)

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Application Process

Investigational Medicinal Product Dossier (IMPD)

- Details of Drug Substance and Drug Product
  - Manufacture
    - List of all facilities involved
    - Detailed description of process
  - Testing
  - Packing
    - Packaging materials
    - Primary Contact
    - Labeling
- Must include a QP Declaration
- Must include stability data to support proposed shelf life
- Can include TSE/BSE statement

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Product Specification File

You are required to have a Product Specification File

- **EudraLex - Volume 4, Annex 13, section 9 gives an overview of the required content.**

This is a reference file containing, or referring to files containing, all the information necessary to draft the detailed written instructions on manufacture, packaging, In-process control testing, analytical testing, batch release and shipping of an investigational medicinal product

The contents of the PSF will vary according to the phase of the Clinical Trial.

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Product Specification File – Some Specifics

Approved label copy in accordance with Annex 13

Where the Clinical Trial is being conducted in countries within the EU which speak different languages, the labels must be translated by an authorized translator and written proof of the correctness; accuracy; compliance of the translated label to Annex 13 as well as specific country regulatory requirements must be provided.

Randomization and randomization codes

Storage and shipment conditions Typically found within the IMPD

Appropriate validation data

Testing Requirements

Stability data

Shelf Life

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Other Clinical Trial Documentation

Technical (Quality) Agreement

•Must be compliant with Chapter 7 of EudraLex - Volume 4 covering outsourcing activities and detailing roles and responsibilities of contract giver and receiver.

•The Technical Agreement should be finalised and signed off as early in the process as possible as this eliminates confusion over responsibility.

•Batches will not be released if a Technical Agreement is not in place.

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In conclusion …

Confirm with your Clinical group as early as possible whether sites in the ROW, and specifically, the EU will be used.

The slightest indication – contact and secure the services of a QP.

Treat the QP as part of your team and involve them in all aspects of your interactions within the EU – in this way you will assure the best, smoothest and quickest start to and continuation of your trial in the EU.

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Thank you for your attention

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